

Analytic Approach to Activity-dependent Adaptive Boolean Networks

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Abstract

We propose new activity-dependent adaptive Boolean networks inspired by the *cis*-regulatory mechanism in gene regulatory networks. We analytically show that our model can be solved for stationary in-degree distribution for a wide class of update rules by employing the annealed approximation of Boolean network dynamics and that evolved Boolean networks have a preassigned average sensitivity that can be set independently of update rules. In particular, when it is set to 1, our theory predicts that the proposed network rewiring algorithm drives Boolean networks towards criticality. We verify that these analytic results agree well with numerical simulations for four representative update rules. We also discuss the relationship between sensitivity of update rules and stationary in-degree distributions and compare it with that in real-world gene regulatory networks.

1 Introduction

Boolean networks (BNs) [12] were originally proposed as a model of gene regulatory networks (GRNs) by S. Kauffman in 1969 [23]. Since then, it also has been used as a useful representation for modeling other complex systems such as neuronal networks [26] and social networks [37]. Although Boolean abstraction of real-world complex systems ignores fine details of them, it enables us to study some important aspects of their generic features. One such feature of BNs is the phase transition between ordered phase and disordered phase [10]. It has often been argued, but still is controversial, that real-world living systems such as GRNs and neuronal networks adjust their dynamical behavior towards the boundary between the two phases, criticality [4, 40, 3, 36, 51]. The advantages of criticality also have been studied: Optimal computational ability [5, 15], maximal sensitivity to external stimuli [25], maximal memory capacity [17] and so on.

So far, many plausible theoretical models of network self-organization towards criticality have been proposed although the exact mechanisms in gene regulatory or neuronal networks have not yet been known. For example, the following literatures discuss biologically inspired mechanisms: Hebbian learning [6, 46], spike-timing dependent plasticity [34, 45], dynamical synapses [29, 30] and homeostatic plasticity [13] for neuronal networks and local control of feedback loops [32] and adaptation towards both adaptability and stability [27] for gene regulatory networks. Such models have been collectively called adaptive networks, in which network structure and network state coevolve, and have been paid much attention recently [16, 47]. The study of adaptive networks originates from the work by Bornholdt and Rohlf [7], which is also motivated by a preliminary work on the relationship between network structure and network state [8]. They showed that a simple activity-dependent rewiring rule based on measurement of local dynamics drives random threshold networks towards criticality by numerical simulation. The model has been extended to different situations: Liu and Bassler [31] reported that the activity-dependent rewiring rule drives random Boolean networks towards criticality by numerical simulation. Recently, this model was extended to networks with modular structure [14]. In spite of the structural constraint, self-organization towards criticality was shown to be preserved. Rohlf introduced an activity-dependent threshold change into the original Bornholdt-Rohlf model [42]. In his model, the threshold change and rewiring are switched stochastically. It was shown that the adaptive thresholds yield a new class of self-organized networks. However, it was confirmed numerically that networks still evolve towards criticality in the large size limit. In summary, these previous works based on numerical simulation suggest that the activity dependent rewiring rule robustly drives networks towards criticality in different conditions.

However, in these adaptive Boolean network models, no analytic approach has been reported so far to the best of the author’s knowledge. One reason for this would be the fact that the definition of activity is dependent on attractors which are usually avoided to discuss the phase transition of Boolean networks in the limit of large system size [10]. In the activity-dependent rewiring rule of Bornholdt and Rohlf [7], a node is defined to be active if it does not change its state on the attractor reached from a random initial condition. Otherwise, the node is said to be static. The rewiring rule is as follows: The active node loses one of its incoming link randomly and the static node acquires a new incoming link randomly. Indeed, it seems that the activity on attractors is crucial for self-organization towards criticality. Bornholdt and Rohlf [7] numerically identified a first-order-like transition of the frozen component defined as the fraction of static nodes and argued that this transition is the main mechanism of robust self-organization of networks towards criticality.

In this paper, we propose a new activity-dependent adaptive Boolean network model inspired by the *cis*-regulatory mechanism of real-world GRNs in which activity does not dependent on attractors but is defined by typical states that will be defined in Sec. 2. By this change of the definition of activity, we

expect that our model admits analysis based on a mean-field theory called the annealed approximation in the limit of large system size. In the following, we show that our model can be solved for stationary in-degree distribution for a wide class of update rules to which the annealed approximation of the Boolean dynamics is applicable. At first sight, one would suspect that our network rewiring rule is designed towards a desired result, namely, criticality. However, it turns out that whether our model can self-organize towards criticality depends on a parameter of our network rewiring rule independent of update rules. We analytically show that the average sensitivity of stationary BN dynamics is equal to the parameter. Thus, only when the value of the parameter is set to 1, we expect that BNs evolve towards criticality. The analytic result is verified by numerical simulation in four representative update rules. We also discuss the relationship between sensitivity of update rules and the decay rate of stationary in-degree distributions and compare it with that in real-world GRNs.

2 Model

Boolean networks (BNs) consist of a directed network with N nodes that can take two states 0 and 1. The state of node i at time step t is denoted by $x_i(t)$ and is updated by a rule f_i selected from a given ensemble of Boolean functions \mathcal{E}_i :

$$x_i(t+1) = f_i(\mathbf{x}_i(t)), \quad (1)$$

where $\mathbf{x}_i(t) = (x_{j_1}(t), \dots, x_{j_{k_i}}(t))$ and j_1, \dots, j_{k_i} are nodes from which node i receives inputs. The number of inputs k_i is called in-degree of i . In this paper, all nodes are updated simultaneously. We also assume that the ensemble of Boolean functions \mathcal{E}_i associated with node i only depends on its in-degree k_i .

Our activity-dependent rewiring rule for network evolution is different from those proposed in previous work [7, 31] in the following two respects. First, both nodes and arcs can be selected at each time step of network evolution, in contrast to the previous models where only nodes are assumed to be selected. Second, we consider activity of arcs rather than that of nodes. In the previous models, activity of a selected node is measured by time-averaging its state value along a reached attractor and the decision whether the selected node gets a new incoming arc or loses an existing arc is made depending on the value of activity. In our model, when a node is selected, the node gets a new incoming arc. On the other hand, when an arc is selected, it is deleted when it is active. Here, activity of the arc is evaluated by the response of the target node i to perturbations on the arc given a *typical state*. That is, given an input $\mathbf{x}_i = (x_{j_1}, \dots, x_{j_{k_i}})$ sampled randomly from a collection of states after sufficiently long time steps starting from a random initial condition, the arc is said to be active if $f_i(\mathbf{x}_i) \neq f_i(\tilde{\mathbf{x}}_i)$ where $\tilde{\mathbf{x}}_i = (\tilde{x}_{j_1}, \dots, \tilde{x}_{j_{k_i}})$ is given by $\tilde{x}_{j_l} = 1 - x_{j_l}$ if j_l is the source of the selected arc and $\tilde{x}_{j_l} = x_{j_l}$ otherwise.

These modifications are motivated by the following biological consideration: Deletion of an arc in a GRN of an organism can be caused by mutations in *cis*-regulatory elements (CREs) [39, 52] of a gene that are nearby non-coding regions of DNA where a number of proteins called transcription factors (TFs) that are themselves products of other genes can bind. TFs regulate expression of the gene by increasing or decreasing the frequency of transcription initiation. If mutations in existing CREs of a gene change the binding pattern of TFs and the expression level of the gene, it could result in undesirable behavior of the organism and the corresponding arcs in its gene regulatory network are deleted in an evolutionary time scale [44]. On the other hand, mutations in a non-coding region of DNA within functional interaction range that is not involved in existing CREs could give rise to binding of a new TF. This means addition of a new incoming arc to the node representing the gene. Thus, nodes in a GRN can be conceived as carrying capacity to accept new incoming arcs incarnated by non-coding regions of DNA rather than coding DNA. In summary, when considering rewiring of a GRN, it is natural to treat nodes and arcs on the same footing because the physical basis of them is the same.

In detail, our algorithm for network evolution in this paper is as follows:

- (i) An initial BN with a given ensemble of Boolean functions is generated. The in-degree of each node is sampled from a Poisson distribution with mean k_0 and the source of each arc is chosen randomly.
- (ii) The state of the BN is evolved from a random initial state for sufficiently long time steps to find a typical state. For any BN of finite size N , its state trajectory eventually falls onto an attractor. Hence, it is ideal to choose a state randomly from the attractor. However, when numerically simulating the model, it is difficult to find an attractor in a reasonable time if the BN is in the disordered phase. For efficient numerical simulation, we limit the maximum length of attractors to be detected as T . If no attractor is found within $2T + T'$ time steps, the last T steps are stored and a state is chosen randomly from the T states. In this paper, we set $T = 1000$ and $T' = 100$. We expect that this way of sampling a state approximates that of sampling from true typical states in the limit of large N because correlations between nodes are negligible for $N \gg 1$ if the underlying network is locally tree-like and thus whether a state is on an attractor or not does not matter if it is reached after many time steps from a random initial state [12]. Indeed, this expectation accommodates to the assumptions of the mean-field theory used in Sec. 3 and we will see that the numerically obtained in-degree distributions by this network rewiring algorithm agree well with the theoretical predictions based on the mean-field theory.
- (iii) A particular node or a particular arc is chosen with probability π_n or π_a , respectively. Here, we fix the ratio $\sigma := \pi_n/\pi_a$ throughout the network evolution. If a node is chosen, then a new incoming arc is added to the node. The source of the new arc is chosen uniformly at random. If an arc is

chosen, then its activity in the state chosen in step (ii) is assessed. If the arc is active, then it is deleted. Otherwise, do nothing.

(iv) The Boolean function on the chosen node or the target of the chosen arc in step (iii) is re-assigned following the given ensemble of Boolean functions.

(v) Go back to step (ii).

The steps (ii)-(v) constitute time unit of network evolution. We call it *epoch* after [31]. Note that $\pi_n N + \pi_a z(e)N = 1$ should hold for all epoch e where $z(e)$ is the average in-degree of the underlying directed network of BN at epoch e . Thus, $\pi_n = \sigma/[(\sigma + z(e))N]$ and $\pi_a = 1/[(\sigma + z(e))N]$.

In each epoch, the network topology and Boolean functions assigned are fixed as in typical applications of BNs for modeling real-world complex systems. Thus, in the above model, the time scale separation between BN dynamics and network evolution is taken for granted.

3 Analytic results

In this section, first we develop a general mean-field theory of network evolution that can be applied to any update rule which satisfies certain conditions mentioned below. Second, we apply the analytic result derived from the mean-field theory to four update rules that have been paid attention in the literature.

3.1 Mean-field theory

If the large system size limit $N \rightarrow \infty$ is taken and the underlying directed network is random networks with a specified degree distribution $P(k, l)$ [35], where $P(k, l)$ is the probability that a randomly chosen node has in-degree k and out-degree l , the stability of BN dynamics can be analyzed by a mean-field theory so-called annealed approximation [10, 28]. In the annealed approximation, correlations between nodes are neglected. This is manifested as the following ansatz taken in the mean-field calculation of BN dynamics [12]: The sources of incoming arcs to a node are chosen randomly at each time step and the Boolean functions are also re-assigned randomly at each time step.

We apply the annealed approximation to BN dynamics in each epoch and assess its stability. For this purpose, we need to calculate sensitivity of Boolean functions selected from a given ensemble for each input [48]. Let $\lambda_{k,j}$ be the probability that the output of an assigned Boolean function with k inputs changes when j -th input is flipped for $1 \leq j \leq k$. We put $\lambda_k := \sum_{j=1}^k \lambda_{k,j}$. In general, $\lambda_{k,j}$ depends on the fraction b_t of nodes with state 1 at time step t . b_t evolves by the following equation

$$b_{t+1} = \sum_k \beta_k(b_t) P_{\text{in}}(k), \quad (2)$$

where $\beta_k(b_t)$ is the probability that the output of a node with k inputs is 1 at time step $t + 1$ and $P_{\text{in}}(k) = \sum_l P(k, l)$ is the in-degree distribution. Although Eq. (2) can have periodic or chaotic solutions depending on update rules [12], we only consider the case that Eq. (2) has a unique stable stationary solution b^* in the following.

Now let us suppose that the dynamics of a BN settle down to the stationary regime and apply a small perturbation. Let \tilde{d}_t be the fraction of damaged inputs at time step t . That is, \tilde{d}_t is the probability that the source node of a randomly chosen arc is flipped. Neglecting the higher order terms of \tilde{d}_t , we obtain

$$\tilde{d}_{t+1} = \lambda \tilde{d}_t \quad (3)$$

for the time evolution of \tilde{d}_t by a similar reasoning with previous work [28, 49], where $\lambda = \sum_{k,l} \frac{lP(k,l)}{z} \lambda_k$ which we call *average sensitivity*, $z = \sum_k k P_{\text{in}}(k)$ is the average in-degree and λ_k is evaluated at b^* . Let d_t be the fraction of damaged nodes at time step t . Since $d_{t+1} = \bar{\lambda} \tilde{d}_t$ where $\bar{\lambda} = \sum_k P_{\text{in}}(k) \lambda_k$, d_t also follows Eq. (3). When in-degree and out-degree are independent as we expect for networks evolved by the proposed network rewiring algorithm, we have

$$\lambda = \bar{\lambda} = \sum_k P_{\text{in}}(k) \lambda_k. \quad (4)$$

When $\lambda < 1$, d_t dies out eventually and the dynamics are said to be ordered or stable. If $\lambda > 1$, d_t grows exponentially at first and the dynamics are said to be disordered or unstable. $\lambda = 1$ is the boundary between the two cases and the dynamics are said to be critical.

Now let us write down the equation for the time evolution of in-degree distribution by assuming the annealed approximation for the dynamics of BN at each epoch. Let $P_{\text{in}}(e, k)$ be the in-degree distribution at epoch e . According to the proposed network rewiring algorithm, we have

$$P_{\text{in}}(e+1, k) = (1 - \pi_n - \pi_a \lambda_k) P_{\text{in}}(e, k) + \pi_n P_{\text{in}}(e, k-1) + \pi_a \lambda_{k+1} P_{\text{in}}(e, k+1) \quad (5)$$

for $k \geq 1$ and

$$P_{\text{in}}(e+1, 0) = (1 - \pi_n) P_{\text{in}}(e, 0) + \pi_a \lambda_1 P_{\text{in}}(e, 1). \quad (6)$$

In order to iteratively solve Eqs. (5) and (6), in each iteration one must calculate λ_k which is in general a function of b^* , which in turn depends on the entire in-degree distribution at epoch e through Eq. (2). In addition, π_n and π_a are functions of average in-degree $z(e)$. A stationary solution $P_{\text{in}}^s(k)$ of Eqs. (5) and (6) should satisfy

$$\pi_n P_{\text{in}}^s(k) = \pi_a \lambda_{k+1} P_{\text{in}}^s(k+1) \quad (7)$$

for $k \geq 0$ if it exists. When the stationary solution exists, we obtain

$$\lambda = \pi_n / \pi_a \quad (8)$$

by substituting Eq. (7) into Eq. (4). Thus, we predict that we can control the stability of evolved BNs by adjusting the ratio $\sigma = \pi_n / \pi_a$ which we call *target average sensitivity* (TAS) hereafter. Note that σ can be given independently of update rules. In particular, when $\sigma = 1$, that is, when a node or an arc is selected uniformly at random, the proposed network rewiring algorithm is expected to drive BNs towards criticality.

Eq. (7) is solved by

$$P_{\text{in}}^s(k) = P_{\text{in}}^s(0) \sigma^k \left(\prod_{l=1}^k \lambda_l \right)^{-1}. \quad (9)$$

If $\lambda_k / k^\nu = \alpha + O(k^{-1})$ for some $\alpha > 0$ and $\nu \geq 0$ and additionally if $\alpha\sigma < 1$ in case of $\nu = 0$, then we have $P_{\text{in}}^s(k) \propto Q(k; \alpha\sigma, \nu)$ as $k \rightarrow \infty$. Here, $Q(k; \mu, \nu) = [\mu^k / (k!)^\nu] / Z(\mu, \nu)$ is a Conway-Maxwell-Poisson (CMP) distribution [9] and $Z(\mu, \nu) = \sum_k \mu^k / (k!)^\nu$. Note that $Q(k; \mu, \nu)$ is a Poisson distribution for $\nu = 1$ and is an exponential distribution for $\nu = 0$ and $\mu < 1$. When $\nu = 0$ and $\alpha\sigma \geq 1$, then $Z(\alpha\sigma, \nu)$ diverges and we will not have a stationary solution for Eqs. (5) and (6).

3.2 Examples

In this subsection, we apply the analytic result presented in Sec. 3.1 to four ensembles of Boolean functions:

- (a) Biased functions (BF) [10]: All Boolean functions with k_i inputs are weighted with bias p . The value of output of f_i is assigned to be 1 with probability p or 0 with probability $1 - p$ for each input \mathbf{x}_i .
- (b) Threshold functions (TF) [43]: Only threshold functions are considered. $f_i(\mathbf{x}_i) = 1$ if $\sum_{l=1}^{k_i} w_{j_l i} (2x_{j_l} - 1) + h_i \geq 0$ or 0 otherwise, where $\mathbf{x}_i = (x_{j_1}, \dots, x_{j_{k_i}}) \in \{0, 1\}^{k_i}$ and $w_{j_l i} = \pm 1$ with equal probability. In the following, we only consider the case $h_i = 0$ for all i .
- (c) Heterogeneous biased functions (HBF) [41]: In this update rule, we allow the bias of BFs to depend on in-degree. That is, a BF with bias p_{k_i} is selected for node i with in-degree k_i .
- (d) Nested Canalizing functions (NCF) [22]: A nested canalizing

function is given by

$$f(\mathbf{x}_i) = \begin{cases} s_1 & \text{if } x_{j_1} = c_1 \\ s_2 & \text{if } x_{j_1} \neq c_1 \text{ and } x_{j_2} = c_2 \\ s_3 & \text{if } x_{j_1} \neq c_1 \text{ and } x_{j_2} \neq c_2 \text{ and } x_{j_3} = c_3 \\ \vdots & \\ s_{k_i} & \text{if } x_{j_1} \neq c_1 \text{ and } \dots \text{ and } x_{j_{k_i}} = c_{k_i} \\ s_d & \text{otherwise} \end{cases} \quad (10)$$

for $\mathbf{x}_i = (x_{j_1}, \dots, x_{j_{k_i}}) \in \{0, 1\}^{k_i}$, where $c_l \in \{0, 1\}$ is the canalizing value for input from node j_l and $s_l \in \{0, 1\}$ is the corresponding output value for $l = 1, \dots, k_i$. Here, we consider a weight on NCFs defined by the following parameters [38]: $s_l = 1$ with probability a and $c_l = 1$ with probability c for $l = 1, \dots, k_i$, and $s_d = 1$ with probability d .

The formula of λ_k for BFs, TFs and HBFs are given by $\lambda_k = 2p(1-p)k$, $\lambda_k = k2^{-(k-1)}\binom{k-1}{\lfloor k/2 \rfloor} \sim \sqrt{2/\pi}/\sqrt{k}$ [43] and $\lambda_k = 2p_k(1-p_k)k$, respectively. For these three rules, λ_k is independent of b^* . However, λ_k of NCFs depends on b^* . We have $\beta_k(b_t) = a + (d-a)(1-\gamma(b_t))^k$ in Eq. (2) where $\gamma(b_t)$ is the probability that a randomly chosen input is at its canalizing value [38]. λ_k of NCFs is shown to be $\lambda_k = (1-\eta)(1-(1-\gamma(b^*))^k)/\gamma(b^*) + k(1-\gamma(b^*))^{k-1}(\eta-\eta_0) \sim (1-\eta)/\gamma(b^*)$ when $0 < \gamma(b^*) < 1$, where $\eta = a^2 + (1-a)^2$ and $\eta_0 = ad + (1-a)(1-d)$ at stationarity [38].

By substituting λ_k into the right-hand side of Eq. (9), we obtain stationary in-degree distributions. For BFs, we get a Poisson stationary in-degree distribution $P_{\text{in}}^s(k) = e^{-z_s} z_s^k / k!$ with the stationary average in-degree $z_s = \sigma/[2p(1-p)]$. The stationary in-degree distribution for TFs is asymptotically equal to a CMP distribution with $\nu = 1/2$. HBFs have different stationary in-degree distributions depending on the functional form of p_k . For NCFs, the stationary in-degree distribution is asymptotically equal to an exponential distribution provided that $0 < \gamma(b^*) < 1$ and $\sigma(1-\eta)/\gamma(b^*) < 1$ where b^* satisfies $b^* = \sum_k \beta_k(b^*) P_{\text{in}}^s(k)$.

4 Numerical results

We compared analytic results with numerical simulations for the above four ensembles of Boolean functions. We simulated evolution of BNs with $N = 200$ for three different values of TAS: $\sigma = 0.95, 1.00$ and 1.05 . Parameters used are $p = 0.7$ for BFs, $p_k = (1 + \sqrt{1 - 2q_k})/2$ with $q_k = 1/2$ if $1 \leq k \leq 3$ and $q_k = 2/k$ if $k \geq 4$ for HBFs (thus, we have $\lambda_k = 2$ for $k \geq 4$) and $a = 1/3$, $c = 0.95$ and $d = 0$ for NCFs.

Fig. 1 shows time evolution of the average sensitivities for each update rule from five different initial average in-degree $1 \leq k_0 \leq 5$. For each pair of values of σ and k_0 , 100 realizations were averaged. In

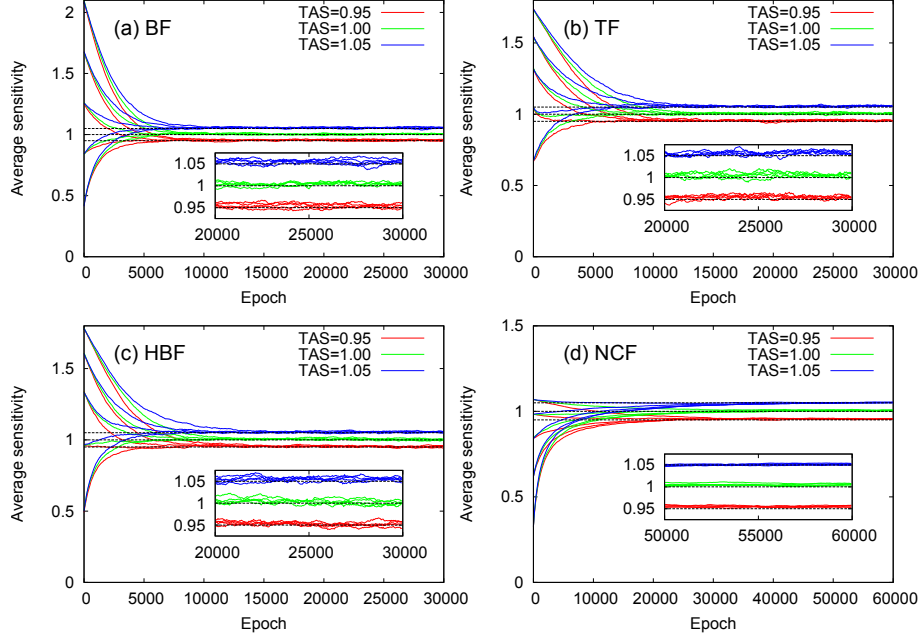


Figure 1: Time evolution of the average sensitivities for (a) BFs, (b) TFs, (c) HBFs and (d) NCFs. Insets are enlarged views from epoch 20000 to 30000 for the first three update rules and that from 50000 to 60000 for NCFs. BNs with NCFs were simulated for a longer period because their convergence is slower than the others.

Fig. 1, the average sensitivity of a BN at epoch e was calculated by Eq. (4) with a numerical in-degree distribution at epoch e and analytic values of λ_k . We can clearly see that the average sensitivities approach to given values of σ independent of k_0 .

The numerical stationary in-degree distributions agree well with the theoretical predictions (Eq. (9)) for all three values of TAS σ (Fig. 2). Here, they were obtained by averaging numerical in-degree distributions over last 10000 epochs in Fig. 1 of 100 realizations for each k_0 .

Finally, we verified numerically that Eq. (3) (with replacing \tilde{d}_t and \tilde{d}_{t+1} by d_t and d_{t+1} , respectively) holds in evolved BNs for all three values of TAS σ by constructing so-called Derrida plots (Fig. 3) [11]. Derrida plots show the fraction of damaged nodes d_{t+1} at time step $t + 1$ as a function of the fraction of damaged nodes d_t at time step t . In Fig. 3, the value of d_{t+1} was averaged over 200 states of 500 realizations of evolved BNs (those at the last step in Fig. 1) for each value of d_t . We can see that for all three values of TAS, the slope at the origin agrees well between numerical calculations and theoretical predictions. In constructing Derrida plots numerically, a subtlety arises when λ_k depends on b^* as in case of NCFs. For BFs, TFs and HBFs, we can choose a random state and randomly flip its fraction of d_t nodes to compute d_{t+1} because λ_k is independent of b^* in these update rules. On the other hand, for NCFs, we must choose a typical state and then randomly flip its fraction of d_t nodes. It was predicted that this procedure produces the correct slope at the origin of Derrida plots [24]. However, in order for

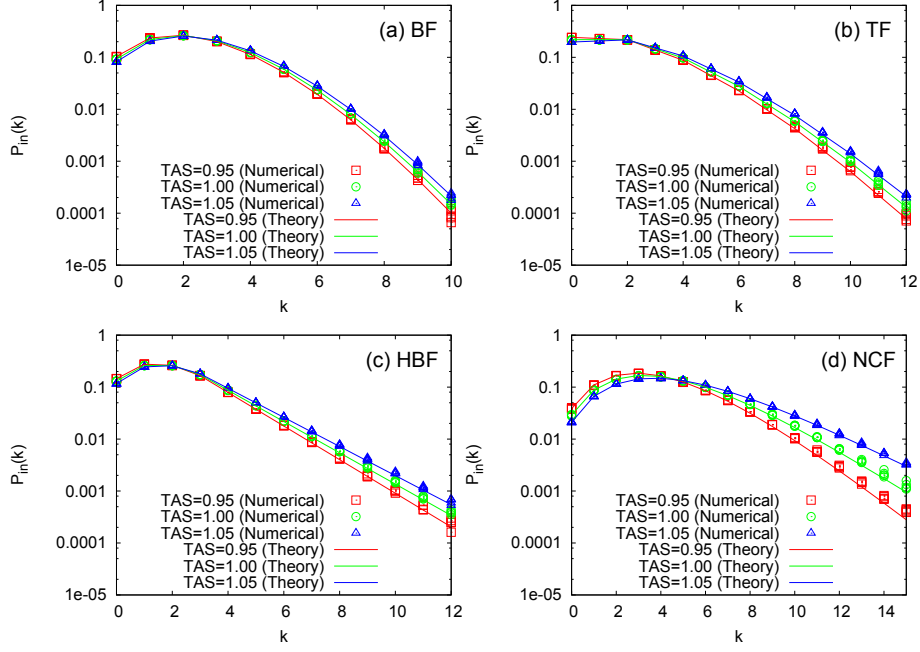


Figure 2: Comparison between numerical stationary in-degree distributions (symbols) and theoretical stationary in-degree distributions (lines) for (a) BFs, (b) TFs, (c) HBFs and (d) NCFs.

a Derrida plot to be correct for larger values of d_t , the perturbed state must also be a random sample of typical states (This does not guarantee that the Derrida plot is correct over all the range of d_t as shown in [24]). Here, we are interested in only the slope of the Derrida plots at the origin. Hence, it suffices for our purpose to adopt the above procedure.

5 Discussion

In this paper, we proposed a new activity-dependent adaptive Boolean network model and presented its analytic solutions for stationary in-degree distribution by employing the annealed approximation of Boolean dynamics. We showed analytically that stationary BNs evolved by the proposed network rewiring algorithm have in-degree distributions whose average sensitivity is equal to TAS and verified the analytic solutions agree well with numerical simulations for four representative update rules. We emphasize that TAS can be given independently of update rules. In particular, if it is set to 1, BNs evolves towards criticality for all values of parameters of a given update rule.

In previous work [20, 33], network self-organization towards criticality has been explained by the self-organized criticality picture [2, 21]. That is, criticality is achieved by slowly adding links in the subcritical phase and rapidly deleting links in the supercritical phase of an absorbing transition of network activity. In particular, Droste et al. [13] analytically demonstrated this mechanism based on the pair-approximation of the network activity dynamics. They showed that two different time-scale separations are necessary

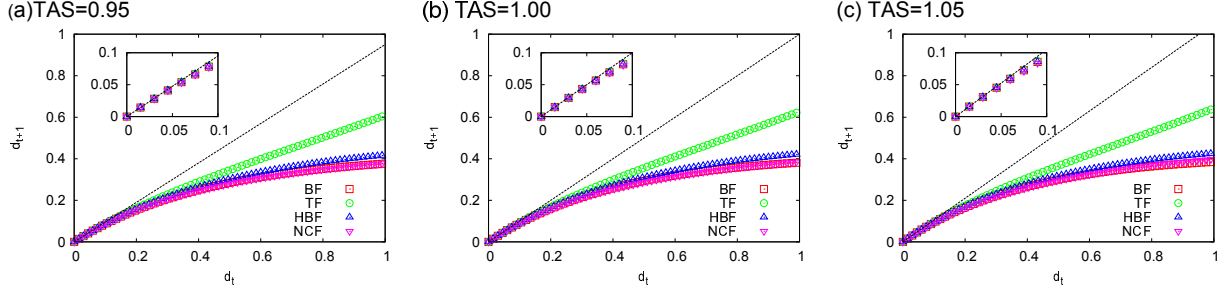


Figure 3: The fraction of damaged nodes d_{t+1} at time step $t+1$ as a function of the fraction of damaged nodes d_t at time step t for (a) $\sigma = 0.95$, (b) $\sigma = 1.00$ and (c) $\sigma = 1.05$. Dotted lines have a slope equal to σ . Insets are enlarged views of the region $0 \leq d_t, d_{t+1} \leq 0.1$.

to realize self-organization towards criticality: one is that between state dynamics on networks and topological changes of networks and the other is that between deletion of links and addition of links. In our model, the former time-scale separation is incorporated. However, the latter does not hold because the ratio of the probability of link addition to that of link deletion is finite. Thus, the self-organized criticality picture seems not to hold. In our model, the criticality is realized by stochastically balancing the mutually opposed processes, addition and deletion of links.

In previous work on activity-dependent adaptive Boolean networks, influence of the update rule on the structure of evolved networks is assessed by only numerical simulations [31, 44]. In our model, we have a simple relationship between the sensitivity of update rules represented by λ_k and the stationary in-degree distribution as shown above. Although our model is parsimonious, it is worth to compare our result with real-world GRNs. The in-degree distribution of the prokaryote *Escherichia coli* is best fitted by a Poisson distribution, whereas that of the eukaryote *Saccharomyces cerevisiae* is best fitted by an exponential distribution [1]. As for update rules, NCFs were introduced to model the yeast GRN [22] because NCFs are found abundantly in eukaryotic GRNs by an extensive literature study [18]. On the other hand, the analysis by Balleza et al. [3] suggested that BFs are enough to model the GRN of *E. coli*. They modeled several real-world GRNs including the bacterium GRN by biased functions to reveal whether they operate close to criticality or not and showed that changes in the fraction of canalizing functions for genes with at least 4 inputs do not affect the near critical dynamical behavior of the bacterium GRN. On the other hand, most of genes in the bacterium GRN have at most 3 inputs and canalizing functions are abundant just by chance for such genes [3]. Thus, there is no need for the bacterium to bias the sampling strategy of update rules towards canalizing functions even if they have an evolutionary advantage. Our model predicts Poisson and exponential stationary in-degree distributions for BFs and NCFs, respectively, and thus is consistent with the real-world GRNs.

We are almost ignorant of out-degree distributions in this paper. Under the proposed network rewiring

algorithm, the stationary out-degree distribution becomes a Poisson distribution independent of update rules. This disagrees with real-world GRNs because they have heavy-tailed out-degree distributions [1]. However, we can control the shape of stationary out-degree distribution by modifying step (iii) of the algorithm without changing the value of average sensitivity: selecting the source of a new arc following an appropriate weight depending on the out-degree of each node [19].

Finally, we note that it is an interesting open question whether our model can be extended to the network ensembles to which the semi-annealed approximation of Boolean dynamics [41, 50] is applicable.

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